

## PEMBROLIZUMAB (Keytruda) PACLITAXEL

### INDICATION (ICD10) C50

Check the most recent Blumetq eligibility criteria before prescribing. Blumetq registration required. ([www.england.nhs.uk/publication/national-cancer-drugs-fund-list/](http://www.england.nhs.uk/publication/national-cancer-drugs-fund-list/))

1. The treatment of previously untreated locally advanced unresectable or metastatic triple negative breast cancer in patients with PD-L1 expression test results of immune cell (IC) <1% and a combined positive score (CPS) of 10 or more. PS 0 or 1. (TA801)

### REGIMEN

Days 1, 8 and 15

Premedication 30 minutes prior to infusion\*\*:

Dexamethasone 8mg IV bolus

Chlorphenamine 10mg IV bolus

PACLITAXEL 90mg/m<sup>2</sup> in 250ml\* sodium chloride 0.9% IV infusion over 60 minutes

PEMBROLIZUMAB 400mg in 100ml sodium chloride IV infusion over 30 minutes every 42 days

\* doses 162mg to 600mg in 500ml sodium chloride 0.9%

\*\* If no hypersensitivity reactions after the first two doses, remove pre-medication with dexamethasone, chlorphenamine and H2 antagonist from dose 3 onwards (off-label).

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days

Pembrolizumab every 42 days until disease progression up to maximum 2 years

Paclitaxel until disease progression or unacceptable toxicity

(if one drug needs to be discontinued due to toxicity, the other may continue)

### ANTI-EMETICS

Low risk days 1, 8 and 15

### CONCURRENT MEDICATION REQUIRED

Paclitaxel	Ensure premedication given before paclitaxel
Pembrolizumab	None required

### EXTRAVASATION AND TYPE OF LINE / FILTERS

Paclitaxel – vesicant

Pembrolizumab – neutral

Administer paclitaxel via polyethylene lined administration set with ≤0.22micron filter

Administer pembrolizumab via low protein binding 0.2 to 5micron in-line or add-on filter

Central line

### INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs every week

Neutrophils x 10<sup>9</sup>/L ≥1.0 day 1 (if not delay), ≥1.0 days 8 and 15 (if not omit clinician discretion)

Platelets x 10<sup>9</sup>/L ≥100 day 1 if not delay), ≥100 days 8 and 15 (if not omit paclitaxel clinician discretion)

Thyroid function\* baseline, then every pembrolizumab cycle

Random cortisol baseline, then every pembrolizumab cycle

Random glucose every pembrolizumab cycle

Baseline weight and every cycle

## MAIN TOXICITIES AND ADVERSE REACTIONS

Paclitaxel	(2% risk of severe hypersensitivity) Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
Pembrolizumab	Immune related toxicities

## INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Paclitaxel	DOACs to be used with caution, need dose modifications or to be avoided eg apixaban Clopidogrel interacts with paclitaxel, potentially increasing the concentration of paclitaxel. Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (eg erythromycin, fluoxetine, gemfibrozil) use with caution. inducers (eg rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution.
Pembrolizumab	-

## DOSE MODIFICATIONS

### Non-haematological

Paclitaxel

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

If grade ≥2 neuropathy, consider giving 75% paclitaxel dose

If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

Pembrolizumab

Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline.

If the drug-related toxicity does not resolve to grade 0-1 within 12 weeks after onset of toxicity, discontinuation is recommended.

## Hepatic impairment

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase <10xULN and bilirubin $\leq$ 1.25xULN	no dose reduction
Transaminase <10xULN and bilirubin 1.26-2xULN	Clinician discretion
Transaminase <10xULN and bilirubin 2.01-5xULN	Clinician discretion
Transaminase $\geq$ 10xULN or bilirubin >5xULN	contraindicated

**REFERENCES**

1. SPC
2. Blueteq criteria